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Letter

The role of benznidazole with cyanocobalamin and ascorbic acid in treating the chronic phase of Chagas disease

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Dear Editor,

We were recently intrigued by an article published in *Revista da Sociedade Brasileira de Medicina Tropical*/Journal of the Brazilian Society of Tropical Medicine by Andrade et al., entitled *Clinical and serological evolution in chronic Chagas disease patients in a 4-year pharmacotherapy follow-up: a preliminary study*[1]. The authors presented an interesting investigation of the role of benznidazole (Bnz) in managing the chronic phase of Chagas disease, and concluded that Bnz is beneficial for patients experiencing the chronic phase of Chagas disease. Although Bnz is the current reference drug for the acute phase of Chagas disease, the results are unsatisfactory, given the limited efficacy and toxic side effects, such as vomiting, anorexia, allergic dermopathy, and peripheral polyneuropathy. In contrast, ascorbic acid and cyanocobalamin are over-the-counter drugs that rarely present side effects. Andrade et al.[1] are to be congratulated for conducting such a comprehensive study regarding the significant role of Bnz in treating the chronic phrase of Chagas' disease. To their discussion, we also note the efficacy of Bnz combined with cyanocobalamin and ascorbic acid, which is evident in the results discussed below.

Some studies have reported that levels of ascorbate-dependent antioxidative enzymes, which use the ascorbic acid that exists in infected tissues, are decreased during some parasitic infections, as the parasites use this mechanism to protect themselves from the oxidizing action of reactive nitrogen species and reactive oxygen species (ROS) that are produced by the host's inflammatory cells[2,3].

For example, Marim et al.[4] have reported that orally administered high-dose ascorbic acid can cause the clearance of trypanosomes, especially trypomastigotes. As well, Ciccarelli et al.[5] have demonstrated that cyanocobalamin markedly decreased the motility and growth rate of *Trypanosoma cruzi* epimastigotes, where its cytotoxic action is thought to occur through the generation of ROS. Moreover, ascorbate peroxidase activity is significantly increased by cyanocobalamin, and ascorbic acid is known to intensify the antiparasitic activity of cyanocobalamin. This mechanism of action is likely due to the well-known prooxidant effects of these compounds, which, when combined with transition metal ions (Co, Cu, and Fe), generate ROS[6]. Accordingly, in the study of Ciccarelli et al.[5], the antiparasitic effect of Bnz treatment was further enhanced by the coadministration of cyanocobalamin and ascorbic acid. As well, it has previously be reported that the that treatment of blood infected with *Trypanosoma cruzi* with ascorbic acid, light, and gentian violet effectively prevents transmission of Chagas disease[7].

Thus, we believe that it is worthwhile to assess the effect of Bnz combined with ascorbic acid and cyanocobalamin as a novel therapeutic modality for treating the chronic phase of Chagas disease.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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